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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/699,240	10/31/2003	Phillip Dan Cook	ISIS-5320	3921

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EXAMINER

RILEY, JEZIA

ART UNIT	PAPER NUMBER
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1637

DATE MAILED: 06/21/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/699,240

Applicant(s)

COOK ET AL.

Examiner

Jezia Riley

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-55 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-55 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>12/22/03</u> . | 6) <input type="checkbox"/> Other: ____ |

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 29, 30, 40, 41, 46-55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 46 recites the limitation "Z" in line 2, page 91. There is insufficient antecedent basis for this limitation in the claim.

Claims 47-55 are also rejected because they depend from claim 46.

Claims 29 and 30 and 40, 41 objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. claims 30 and 41 depending from claims 29 and 40 respectively do not specify a further limitation of the subject matter in claims 29 and 40. Since there is no limitation for the R1 moiety, therefore R1 is viewed to be anything hence claims 30 and 41 do no further limit claims 29 and 40 respectively.

Claim Rejections - 35 USC § 102

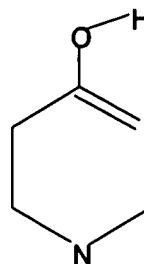
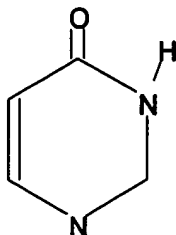
3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

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A person shall

-

(b) the invention
printed
country or in
country, more
of application for



be entitled to a patent unless

was patented or described in a
publication in this or a foreign
public use or on sale in this
than one year prior to the date
patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 1, 2, 4-9, and 17-23 are rejected under 35 U.S.C. § 102(b) as being anticipated by Ajinomoto (JP 2-264792).

The reference shows an oligomeric compound (formula I) on page 1009, having an identical formula to the compound of instant claim 1 for example where Q_1 and Q_2 are linking moieties and/or hydroxyl or protected hydroxyl, Z is methoxy, the base is thymine, and n is 1-100. The reference shows the base having the "X" moiety as a double-bonded oxygen which is well known as one of the tautomeric forms of the base of structure I of instant claim 1. The equilibrium reaction between tautomers can be written as follow:

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5. Claims 1-23 are rejected under 35 U.S.C. § 102(e) as being anticipated by Huie et al. (Patent # 5,470,967).

Huie et al. describe oligonucleotides comprising monomers attached to each other by a linking group. Col. 4-5, disclose a compound of the same formula as described in instant claim 1 for example, where, B is a natural nucleic acid or synthetic modified nucleic acid base which is viewed to include the base of instant claims 1, 10, or 24 where R can be methyl, and L an oxygen which represent thymine. R₁ and Y-M-Z are hydroxyl or protected hydroxyl and linking moieties which are viewed to be inclusive of instant Q₁ and Q₂. A can be H, OH, protected hydroxyl or halogen which is viewed to be inclusive of instant Z. In col. 6, line 64-66, n is at least one up to 200, which is viewed to be inclusive of instant claims 4-6, 12, 13, 19, and 20. Compounds where at least one of the sulfur based linkages of this invention is substantially near at least one terminus of the compound, are expected to be particularly useful (col. 7, lines 3-15) which is viewed to be inclusive of instant claims 9, 16, and 23. And the base of Huie et al. can be a naturally occurring nucleic acid base or synthetic modified base. And as discussed in the 102(b) rejection above, a base having the "X" moiety as a double-bonded oxygen is well known as one of the tautomeric forms of the base of structure I of instant claim 1.

6. Claims 1-23 are rejected under 35 U.S.C. § 102(b) as being anticipated by Matteucci et al. (WO 92/05186).

Matteucci et al. disclose on page 5 an oligomer of the formula (1) where the linking group Q can be a two to four atoms selected from nitrogen, oxygen or sulfur, with the remainder being carbon. R can be F, O-alkyl, and B is independently a purine or pyrimidine residue. Preferred modified internucleoside linkages for Q are shown in Table 1, pages 14-20.

Claim Rejections - 35 USC § 103

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 24, 25, 31-36, 42-45 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Fraser et al. (J. Heterocyclic Chem., Vol. 30, p. 1277, 1993) in view of March (Advanced in Organic Chemistry, pp. 227-229), further in view of Solomons

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(Organic Chemistry, Fifth Edition, p. 433, 1992), and further in view of Uhlmann et al. (Chemical Review, Vol. 90, pp.543-584), Olmstead et al. (J.A.C.S. vol.99, page 4219-4228, 1977) and Sterzycki et al. (J. Med. Chem., Vol. 33, pp.2150-2157).

The Fraser et al. reference discloses the process of synthesizing 2'-thiosubstituted pyrimidine nucleoside by reaction of methanethiol with 2,2'-anhydrouridine. The reaction mixture was heated in a pressure vessel at 60°C for 12 hours (page 1284, col.2, 4th paragraph and page 1285, col.1). However, Fraser et al. do not show the use of alcohol in the presence of a Lewis acid to form the 2'O-substituted pyrimidine. But an acid-catalyzed ring opening by an alcohol is extremely well known in the art of organic synthesis see p 433 of Solomon. The H⁺ catalyst can be considered as a Lewis acid as explained in March page 227: "In the Bronsted picture, the acid is a proton donor, but in the Lewis picture the proton itself is the acid since it has a vacant orbital."

It would have been obvious to someone of ordinary skill in the art at the time the invention was made to synthesize 2'O-substituted pyrimidine nucleoside by reaction of an alcohol in the presence of an Lewis acid with 2,2'-anhydrouridine since this type of reaction has been performed with thiol derivative. Sulfur is directly below oxygen in Group VI of the periodic table. Sulfur and oxygen have chemical similarities and general chemical interchangeability of oxygen and sulfur are well known in the art of organic chemistry (see Olmstead et al. Page 4223, columns 1-2, where the nucleophilicity of CH₃S⁻ is compared to CH₃O⁻). Therefore, one would have been

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motivated to use alcohol as a nucleophile to synthesize 2'-O-substituted nucleoside to increase the stability of the duplex against RNaseH by synthesizing adequate modified nucleotides since this type of modification have shown nuclease resistance thus motivating their use (Uhlmann et al, pages 557-558). Further, amination of uridine nucleoside to obtain cytidine nucleoside is well known in the art of organic chemistry, see for example, Sterzycki et al. page 2151 scheme I and page 2154, col. 2, fourth paragraph, for example.

Double Patenting

9. A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

10. Claims 26-29 and 37-40 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 1-8 of prior U.S. Patent No. 5,760,202. This is a double patenting rejection.

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11. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321© may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

12. Claims 24 and 35 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 5 of U.S. Patent No. 5,760,202 . Although the conflicting claims are not identical, they are not patentably distinct from each other because: claims 24 and 35 of the instant application disclose a process using any Lewis acids claims 1 and 5 of the patent disclose the same method using borate as the Lewis acid. Claim 1 and 5 of the patent are therefore species of claims 24 and 35 of the instant application. The species therefore anticipates the genus because the term Lewis acid encompasses Borate which is a well known and well used Lewis acid in the art of organic chemistry.

13. Claims 1-23 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-23 of U.S. Patent No. 6,222,025.

Although the conflicting claims are not identical, they are not patentably distinct from

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each other because they are both claiming same compound comprising structure I , II or III.

14. Claim 24 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6,642,367. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are both claiming same process for the synthesis of 2'-O-substituted pyrimidine nucleoside comprising a 2-2'-anhydropyrimidine and an alcohol of formula R1-OH.

15. Claim 1 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1-3 of U.S. Patent No. 6,166,197. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are claiming common embodiments but not of the same scope.

17. The reference 47 is duplicate of reference 46 and reference 79 has not been provided by applicants.


18. No claims are allowed.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jezia Riley whose telephone number is 571-272-0786. The examiner can normally be reached on 9:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Monday, June 19, 2006



JEZIA RILEY
PRIMARY EXAMINER